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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/726,160	12/02/2003	Nancy Y. Ip	MLY-2-DIV-CIP	5458

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DORITY & MANNING, P.A.
POST OFFICE BOX 1449
GREENVILLE, SC 29602-1449

EXAMINER	
HARRIS, ALANA M	
ART UNIT	PAPER NUMBER
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/726,160	IP ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *2-6 and 10-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 7-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 December 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/05/04; 04/12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1 and 7-9) in the reply filed on September 6, 2006 is acknowledged. The traversal is on the ground(s) that the inventions are not independent and the subject matter of inventions set forth in Groups II and V are specific in scope, see Remarks, page 4, last two paragraphs. This is not found persuasive because the product of Group I is separate and distinct from the other inventions, particularly the product of Groups II and the method of Group V, which implements an antibody product. These inventions are not useable, nor searchable together as indicated in the Requirement mailed August 4, 2006.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-12 are pending.

Claims 2-6 and 10-12, drawn to non-elected inventions, are withdrawn from examination.

Claims 1 and 7-9 are examined on the merits.

Specification

3. The disclosure is objected to because of the following informality: the brief description of the drawings for Figure 8 does not distinctly note Fig. 8A and 8B and the differences between the two panels as set forth in 37 CFR 1.74, see MPEP § 608.01(f). Correction is required.

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, see page 15. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1 and 7-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The facts to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex Parte Forman,* 230 USPQ 546 (BPAI 1986) and *Ex Parte Wands;* 858 F.2d731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The specification teaches SEQ ID NO: 1, a nucleic acid sequence encodes SEQ ID NO:2, a retinoic acid regulated expression product or retinoic acid regulated nuclear matrix protein (RAMP), see page 2, lines 7-10 and page 8, lines 19-23. The nucleic

acid sequence, SEQ ID NO:1 is also referred to as 8.31 (see page 10, lines 5-8) and its encoded expression product are alleged to have applications:

(1) as a diagnostic marker for the diagnosis of hepatocellular carcinomas (HCC), see page 2, lines 12-14 and page 3, lines 4-12;

(2) in the manufacture of medicaments for the treatment and prevention of Ushers disease and diseases associated with its expression, morphogeny and mitogeny, see page 3, line 28-page 4, line 5 and page 5, lines 18-20); and

(3) in the preparation of recombinant DNA technology purposes.

Several figures show the 8.31 expression in retinoic acid (RA) in several cell types with seemingly no discriminate dissemination between the cell types, see Brief Description of the Drawings on page 6 and the corresponding Figures. Figure 8 shows the expression of 8.31 in the tumor sample from a HCC patient and none in the normal tissues adjacent to the tumor. And Figure 2, Figure 5 and Figure 6 provide data exemplifying expression of 8.31 is down regulated in RA-treated Ntera-s/Da (NT2) human teratocarcinoma cells, KG1 and acute promyelocytic leukaemia cells (HL-60), respectively over a period of days. These *in vitro* treatment of cell lines is not evidentiary or corollary to the treatment and prevention of a disease that affects humans.

Furthermore, it is not clear that the cell lines Applicants have treated are cell types affected by Usher's disease. Applicants have not expounded upon or taught the link between HL-60 cells and Usher's disease. Usher syndrome (USH) or disease is art known to be an autosomal recessive disorder characterized by severe hearing loss or deafness and retinitis pigmentosa, see Reiners et al. (Experimental Eye Research 83:

97-119, 2006). Reiners presents the proteins encoded by the identified USH genes and contemplates gene therapy in the treatment of USH, see page 99, section 2 and page 113, section 5. And while Reiners notes therapeutic approaches show great promise, "[w]hatever therapeutic approaches for USH will be chosen, it is currently necessary to validate them in an animal model that mimics the mutant phenotype of human USH disease and at present no appropriate animal model is available, see page 114, 1st paragraph.

Applicants allude to a link between HCC and the RAMP noting it is detected in over 70% of patient sample at the early stages of HCC, while the normal liver tissue shows very low or undetectable expression of the said protein, see page 8, line 19-page 9, line 8. This observation only seems to provide information on the detection of RAMP in this cell type and does not provide a basis for establishing treatment and prevention.

There is no corollary evidence presented that would substantiate that treatment of HL-60, KG1 or NT2 cells would some how provide a basis that USH or HCC could be treated. Applicants' specification seems to suggest treatment with RA with treat USH and HCC. The information of record in the specification and the state of the art in no way suggestive of treatment with RA would be effective. Based on these observations it would be undue experimentation to use RA in a treatment modality when it is yet to be established the cancer cell types of diseases associated with 8.31 expression. Furthermore, it is not clear from Applicants' disclosure of how the 8.31 gene and its expression product be used as diagnostic tool. The disclosure has not set forth any definitive parameters governing the types to be tested. The specification suggests

that 8.31 serves as a candidate marker for genetic diseases, but that it not substantial evidence supporting the use of 8.31 gene and its encoded product in any treatment regimen for USH, particularly type of USH as suggested in the specification on page 4. The last sentence of Example II on page 10 cites "[t]he expression profile of 8.31in a range of cell types and under a range of conditions has allowed a role for it to be determined." This suggests that Applicants' disclosure is an invitation to develop a treatment regimen for cell types for diseases that are associated with 8.31. No nexus has been established between 8.31 and the treatment of Usher's type II disease and cancer cell types, such as acute promyelocytic leukaemia. High expression of 8.31 in hematopoietic tissues and the correlation that expression of 8.31 is associated with the differentiation of other cancer cell types does not establish a sound basis for treatment as suggested in Applicants' disclosure.

Therefore, in weighing the factors to be considered in determining whether or not the practice of claimed invention would require "undue" experimentation, as set forth in *In re Wands,* 8 USPQ2d 1400 (CAFC 1988) the weight of the analysis clearly favors a finding of "undue" experimentation.

7. Claims 1 and 7-9 are free of the art.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is

(571)272-0831. The Examiner works a flexible schedule, however she can normally be reached between the hours of 7:30 am to 6:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
21 November 2006